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Two hundred forty-two female Wistar rats were observed throughout their life span following 1,000 r hypoxic total-body or partial-body irradiation. Hypoxic radiation with superimposed anesthesia resulted in 67 percent 30 day mortality, compared to 9 percent mortality without anesthesia. Selection of the colony by acute postirradiation deaths did not influence the magnitude of late radiation sequelae as measured by life-shortening. Growth retardation during the second postirradiation year was well correlated with life-shortening. Life-shortening was observed after partial-body irradiation to an extent approximately proportional to the weight of radiated tissue. Nephrosclerosis was not observed unless the upper abdomen was included within the radiation field. Other than nephrosclerosis, a similar incidence of disease was observed at death in control and irradiated rats whether partial-body or total-body irradiated.

Exposure of the total body to sublethal quantities of ionizing radiation has resulted under some conditions in delayed or late sequelae. The tumors, cataracts, and nephrosclerosis observed in rodents after such total-body exposure have generally been ascribed to the direct action of the radiation upon the individual tissues involved by these delayed pathologic changes. In the absence of a specific locus within the body that is clearly dominant in its influence upon aging, the reduced longevity also observed in such total-body radiation studies has usually been interpreted as a collective effect of radiation damage to all the exposed tissues of the body

The development of some of the neoplasms commonly associated with total-body radiation exposure of rodents has been shown in recent years to be influenced by complex indirect mechanisms involving other organs, in addition to the direct action of the radiation upon the tissues of tumor origin. The altered endocrine balance associated with tumors of the ovary, thyroid, and pituitary, and the influence of nonirradiated bone marrow upon the incidence of postirradiation thymic lymphoma are examples of this more systemic aspect of delayed radiation sequelae.

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The *partial-body* irradiation studies reported here were initiated to determine the relative importance of direct local tissue injury and more systemic irradiation changes upon the development of the rodent nephrosclerosis of total-body irradiation. The reduced longevity also observed in these experiments involving radiation of less than the total body also provides some opportunity to evaluate the importance of various segments of the body in radiation-induced experimental aging.

METHODS

The experimental animals were 242 young female Wistar rats, obtained from Carworth farms. Each weighed about 180 gm. They were divided at random into five groups, as indicated in table I. The four irradiated groups received total-body or partial-body exposures to 1,000 r x-radiation delivered in a single dose. The animals were anesthetized with 1.0 ml. of 1:10 intraperitoneal myotal® solution and were in a partially protective hypoxic state from inhalation of a 5.0 percent oxygen, 95 percent nitrogen mixture, as previously described (1), before and during the radiation exposure. The fifth group served as nonirradiated controls and received only a comparable period of hypoxia and anesthesia.

Irradiation factors employed were 250 kv., 15 ma., 0.25 mm. Cu parabolic, 1.0 mm. Al, and 0.21 mm. Cu inherent filters, 35 cm. target-to-object distance, 30 cm.^{2} field size, 1.47 mm. Cu HVL, and 185 r/min. Two simultaneously energized targets were employed, one directed dorsally and the other ventrally.

Radiation was delivered to either the whole body or those portions of the body not protected by the $^5/_{16}$ inch lead shielding referred to in table I. Shielding of the head to the level of the clavicles excluded 11.8 percent of the body weight from the x-ray beam. Upper abdomen shielding, extending from the 13th rib to the lower poles of the kidneys, excluded 18.1 percent of the body weight. Conversely, 81.9 percent of the total body was eliminated from the x-ray field by shielding that permitted irradiation of the upper abdomen only. Proportions of body weight protected by these lead foil shielding procedures were determined by the mean weights of comparable frozen segments of 10 sectioned rat carcasses.

The first group of rats was irradiated when the colony had a mean weight of 180 gm. and, based upon this weight, an estimated age of 102 days. The other three groups of rats were irradiated within the following 27-day period.

After irradiation, rats were housed 4 to a cage in an air-conditioned vivarium and fed Rockland rat diet and tap water ad libitum. Rats that died during the first 30 days post-irradiation are also indicated in table I. These animals were excluded from the study of late radiation effects.

Systolic blood pressure measurements were made at sporadic and infrequent intervals

TABLE I

Initial number and selection of rats for analysis of longevity and incidence of nephrosclerosis following 1,000 r hypoxic total body or partial body x-ray exposure

	Irradiated				Nonirradiated controls	Total
	Extent of lead shielding					
	Head	Upper abdomen	Entire body except upper abdomen	None		
Initial number of rats	36	40	39	79	48	242
Estimated age at radiation in days	107	102	129	109	–	–
Acute deaths during first 30 days	2	2	0	53	0	57
30-day mortality	LD_6	LD_5	LD_0	LD_{67}	–	–
Deaths attributed to later anesthesia	2	0	3	0	1	6
Rats suitable for longevity statistics	32	38	36	26	47	179
Autopsies performed	25	28	32	17	32	134

during the ensuing 27-month survival period. Six rats died as a consequence of the myotal® anesthesia used during these measurements and are also deleted from the long-term survival study. The remaining members of each group comprise those 179 rats deemed suitable for longevity statistics (table I).

On several occasions during the 27 months of postirradiation observation, acceleration of the death rate as a result of epidemic respiratory disease threatened to destroy the colony. At such times all surviving animals of the five groups received penicillin (2,000 units) and streptomycin (0.0025 gm.) subcutaneously, for three consecutive days during the 6th, 8th, 10th, and 13th months postirradiation. All surviving animals also received one dose of mapharsen® (0.2 mg.) and two doses of chloramphenicol (50 mg./kg.) during the 13th month. In addition, the rats receiving radiation only to the upper abdomen received an additional similar 3-day course of penicillin-streptomycin commencing on the fourth day after radiation exposure during the period of acute radiation sickness. No other supportive care of any kind was administered.

Animals died naturally or were killed when death appeared imminent. Autopsies were performed on 134 of the 179 rats of the longevity study. In figures 1 to 4 duration of postirradiation survival is plotted to the nearest half month.

OBSERVATIONS

Degree of selection by 30-day mortality

This study differs from our previous postirradiation studies in that a general anesthesia was added to the conditions of irradiation exposure. With hypoxia and anesthesia combined in this way, a low 30-day mortality ranging from 0 to 5 percent was observed to follow experiments involving shielding of a portion of the body. On the other hand, under these conditions of combined hypoxia and anesthesia, total-body irradiation was followed by a 30-day mortality of 67 percent (table I). This was in contrast to an expected mortality of approximately 9 percent, as observed in several previous studies in this laboratory using the same 1,000 r hypoxic total body exposure without anesthesia (2).

Decrease of longevity

Mean and median postirradiation survival times of the four groups receiving either partial or total-body irradiation were all shorter than the control survival period (table II). Statistically significant differences of mean survival are indicated by brackets between groups at the bottom of the table.[1] Under the conditions of this experiment, it is apparent that significant life-shortening was produced by radiation of less than the entire body.

When the duration of survival of the various groups of table II are equated against the proportion of the total body irradiated in the several experiments, the relationship in figure 1 is obtained. Reduction of life span appears possible directly related in some fashion to the weight of body tissue exposed to the radiation beam. The straight line drawn provides a reasonable fit to the data, but this linear relationship is probably only fortuitous. The reduction of longevity following irradiation of 18.1 percent of the body in the upper abdomen is greater in proportion to the volume of tissue included in the radiation field, but this reduction of longevity is not statistically significant.

Selection by 30-day mortality fails to influence longevity of longer-term survivors

Mean duration of postirradiation survival of the 26 highly selected rats of the totally irradiated group was reduced proportionately below that observed in the nonirradiated controls by an amount similar to that observed in previous studies with the same radiation dose not complicated by high selection from acute 30-day mortality (2). Present data (open circles) are compared with mortality curves from such a previous study in figure 2. In the prior experiment (2) longevity of post-30-day survivors of a 1,000 r radiation exposure lethal to 9.0 percent in 30 days ($LD_{9/30}$) was reduced 39 percent. Mean survival following the $LD_{67/30}$ total-body exposure reported here was 12.0 months as contrasted to 20.5 months in the controls (table II). This represents a similar 41 percent reduction of life span.

[1]Tukey comparison.

The shorter period of survival of both irradiated and control rats in the present study (open circles) as compared to the previous experience (fig. 2) is probably best explained by difference of environment in the two experiments. The longer durations of life in both control and irradiated rats were observed when animals were housed in an isolated basement room removed from other rodents and the attendant risk of transmissible disease associated with proximity of other animals (2). In contrast, the survivors of the present report were housed throughout their life span in a large densely populated air-conditioned vivarium.

Retardation of growth

Growth curves following total-body radiation are indicated by mean body weight of the survivors at approximately monthly intervals in figure 3. Data from the present study (open circles) are again superimposed on the growth data from the 167 rats previously reported (2). Mean total body weight of the postirradiation survivors of the present study at 20 months was approximately 15 percent less than in the controls, as contrasted to the 18 percent reduction of weight observed at 20 months in our earlier study (2).

A selective tendency for the larger irradiated rats of a given colony to die sooner would produce mean weight curves with this shape. Survival of the smallest and largest rats of our irradiated group has been similar, however, and the suppression of mean growth during the second postirradiation year cannot be explained on this basis. This retardation of growth in the irradiated group as measured by the mean

TABLE II

Duration of postirradiation survival after partial-body and total-body hypoxic irradiation with 1,000 r during anesthesia

	Irradiation (1,000 r)				No irradiation
	Lead shielding				
	None	Head	Upper abdomen	Entire body except upper abdomen	
Proportion of body irradiated	100%	88.2%	81.9%	18.1%	0
Number of rats surviving 30 days	26	32	38	36	47
Mean post-irradiation in months	12.0	13.0	12.5	17.0	20.5
Median post-irradiation survival in months	12.0	13.5	14.5	17.5	22.0
Reduction of median postirradiation longevity (percent)	45	39	34	20	0

Bracketed columns indicate significant differences at the 95 percent confidence level.

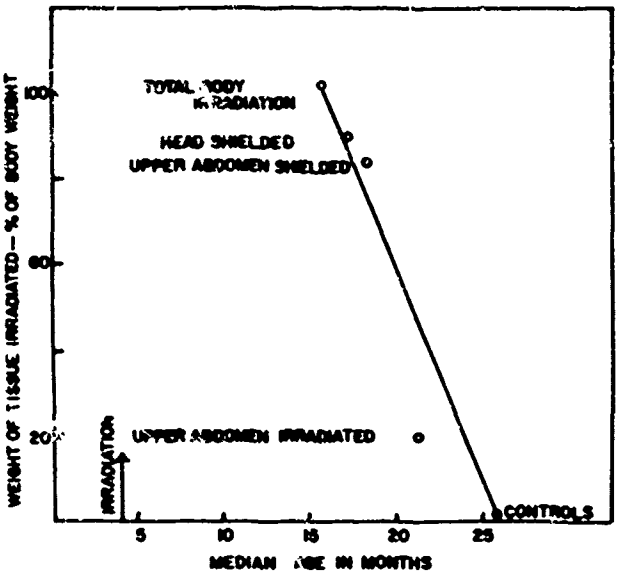

FIGURE 1

Median postirradiation survival following 1,000 r hypoxic total-body or partial-body irradiation. Median survival is plotted as abscissa; percent of body weight within the irradiation field as ordinate.

total body weights of the survivors accurately reflects the growth curve of the average individual rat. Increase in weight during the second postirradiation year is retarded. Loss of 10 to 15 percent body weight often precedes death.

It appears that the selection within the colony brought about by acute deaths occurring within 30 days of the total-body radiation exposure under the conditions of anesthesia and hypoxia of the present study has not altered the composition of the colony as measured by the effects of radiation upon either the process of aging or the capacity for maximum growth. Data from both the present and earlier experiments further suggest that there is an association between the process of aging and the capacity to produce new tissue as measured by increase in body weight.

Longevity and growth in partially irradiated rats

In general, a rough correlation between longevity and capacity to grow also appears in the partially irradiated groups, as revealed in the mean body weight curves in figure 4. The rats with only the upper abdomen irradiated, representing 18.1 percent of the body weight, had the least degree of reduction of median longevity, 20 percent (table II), and the smallest retardation of growth at 20 months (approximately 7 percent). The totally irradiated group was 15 percent smaller than the controls at 20 months. In the other two experiments where 81.9 percent and 88.2 percent of the body were irradiated, weight curves were too closely similar to the weight curve of the totally irradiated rats to be separately interpreted.

AUTOPSY FINDINGS

Complete autopsies were performed on 134 of the 179 rats of the long-term study. With the exception of nephrosclerosis, all groups showed a similar spectrum of disease. Acute inflammations of the lung, pleura, or pericardium were the principal causes of death in the majority of rats of each group. Occasionally peritonitis, acute pyelonephritis, acute otitis media, and purulent distentions of the fallopian tubes were also encountered. The malignant and benign tumors observed are tabulated in table IV and are separately discussed below.

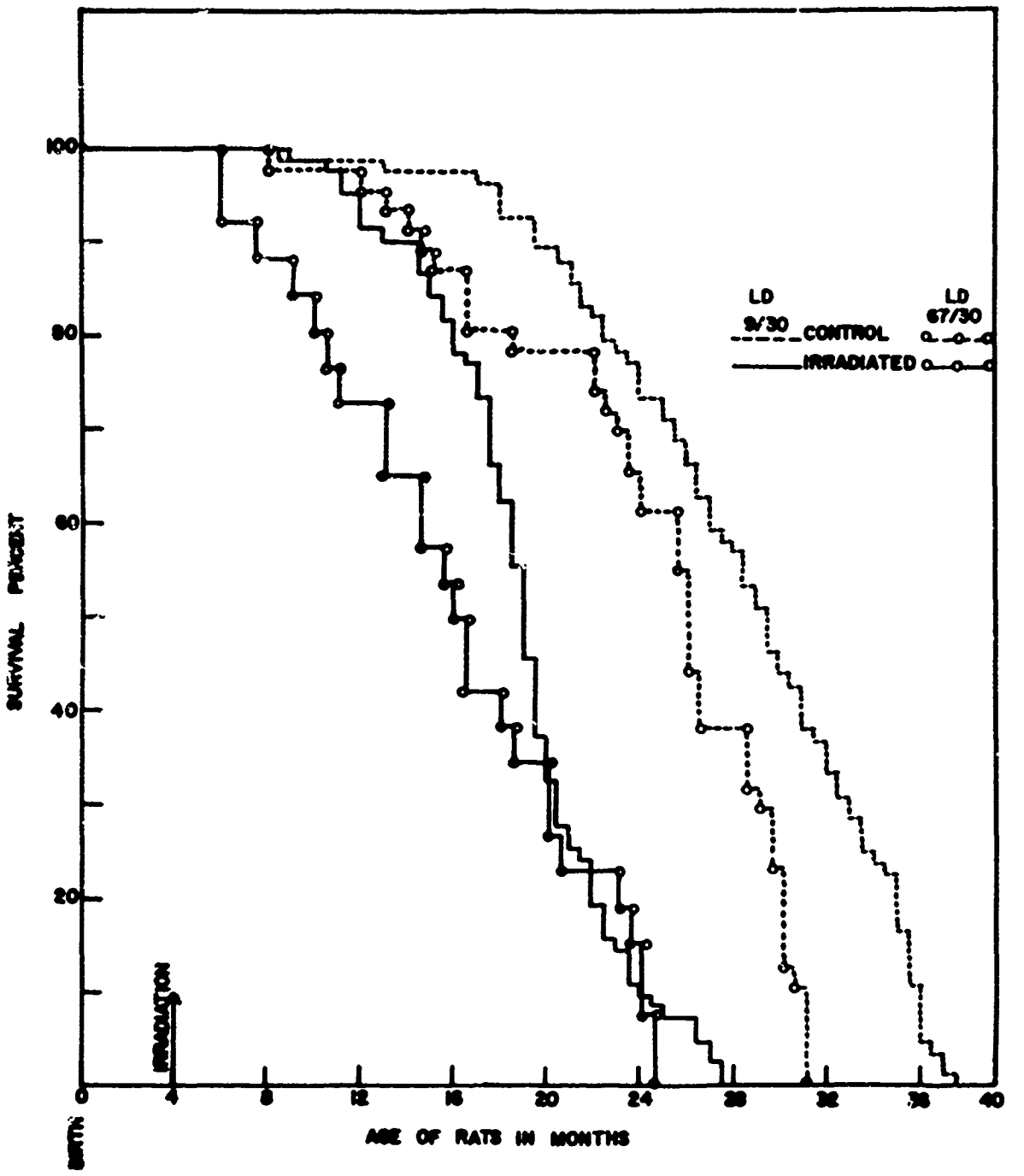

FIGURE 2

Postirradiation and control mortality curves of female Wistar rats after 1,000 r hypoxic irradiation with and without superimposed anesthesia. Open circles indicate control and postirradiation survival after 1,000 r with anesthesia ($LD_{67/30}$); points depict survival after 1,000 r without anesthesia ($LD_{9/30}$).

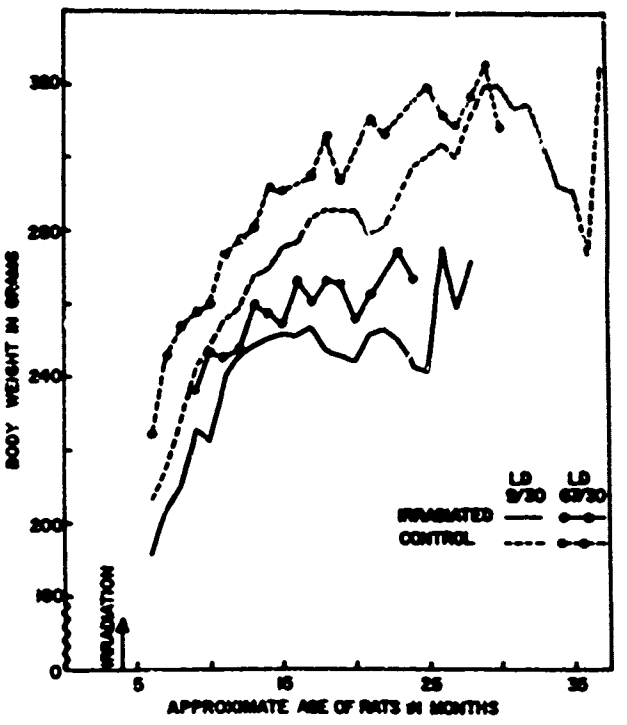

FIGURE 3

Postirradiation and control mean body-weight curves of female Wistar rats after 1,000 r hypoxic irradiation with and without superimposed anesthesia. Open circles indicate control and postirradiation mean body weights after 1,000 r with anesthesia ($LD_{67/30}$); points depict mean body weight after 1,000 r without anesthesia ($LD_{9/30}$).

Many of the older rats also experienced epilation of the head, neck, and dorsum of the trunk. The extent and locus of this epilation bore no relationship to the region of the body within the radiation field.

Prevalence of nephrosclerosis

The incidence of nephrosclerosis in the various experiments is shown in table III. A higher degree of characteristic nephrosclerosis (3, 5) was observed in all three groups where the upper abdomen and kidneys were within the irradiation field.

Most of the liver and spleen, all of the kidneys and adrenals, many loops of bowel, and a portion of the bone marrow were protected from radiation by shielding of the upper abdomen. This shielding procedure eliminated the type of nephrosclerosis characteristic of total-body radiation exposure (3, 5). This absence of radiation-induced renal disease is in contrast to the 56 percent incidence of nephrosclerosis in the head-shielded study and 35 percent incidence in the totally irradiated group. When only the upper abdomen including the renal area was irradiated, 22 percent developed nephrosclerosis. In the latter experiment where 81.9 percent of the body was protected from irradiation, this 22 percent incidence of nephrosclerosis was not significantly less than in other groups also receiving radiation to the upper abdomen, but the renal disease did occur later than in the other two experiments. Animals of this upper abdomen radiation study were also approximately three weeks older at the time of irradiation than the head-shielded and unshielded groups (table I).

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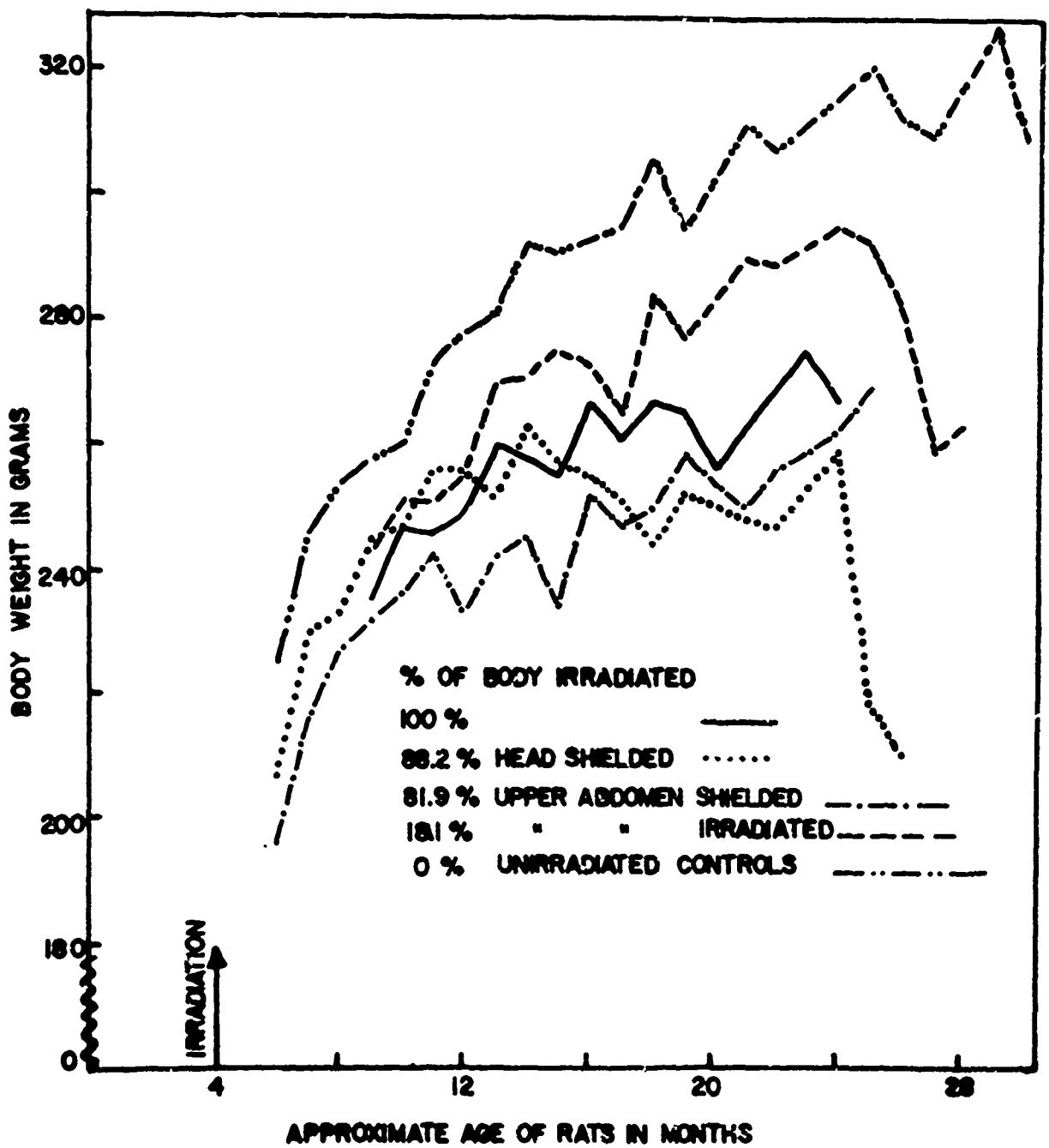

FIGURE 4

Postirradiation and control mean body weight curves of female Wistar rats after 1,000 r hypoxic total-body or partial-body irradiation.

TABLE III

Incidence of nephrosclerosis in partially shielded female Wistar rats compared to rats surviving 1,000 r hypoxic total-body irradiation

Extent of body shielding	Months postirradiation survival										Total	
	2 - 6		7 - 12		13 - 18		19 - 24		25 - 30			
	Neph. deaths		Neph. deaths		Neph. deaths		Neph. deaths		Neph. deaths		Neph. deaths	
Head	0	3	1	3	8	12	5	7	–	–	14	25
Upper abdomen	0	2	0	5	0	12	0	9	–	–	0	28
Entire body except upper abdomen	0	1	0	6	1	9	6	16	–	–	7	32
None	0	0	2	6	4	6	0	5	–	–	6	17
Controls no irradiation	0	1	0	1	0	2	1	12	0	16	1	32

Blood pressure measurements were too infrequent in this study to provide useful data.

Nephrosclerosis as a cause of death

The majority of rats with severe nephrosclerosis die with pneumonia. In the absence of chemical evidence of nitrogenous retention the extent that renal failure may also contribute to death is uncertain. From the histologic appearance of the more severely damaged kidneys renal failure would be anticipated. The majority of the glomeruli are severely sclerosed with complete obliteration of the capillary tufts (3).

On the other hand, the incidence of nephrosclerosis does not correlate well with the median survival or mean survival of the several groups of rats. For example, in the head-shielded study nephrosclerosis was found in 14 of 25 rats. When the upper abdomen alone was shielded the incidence of nephrosclerosis was zero, yet longevity was increased very little (fig. 1). The increase in median survival was roughly proportional to the increased weight of tissue protected from irradiation by the increase in shielding from 11.8 percent to 18.1 percent of the total body weight.

When the upper abdomen alone was irradiated, median survival time was reduced to 17.5 months from 22.0 months in the controls. This reduction of life span is larger than would be expected from the proportional weight of tissue irradiated, as can be seen from the plot in figure 1, but is still not statistically significant. The 17.5 month survival after an 18.1 percent body weight irradiation falls to the left of the line drawn through the other four points. The delayed nephrosclerosis in this upper abdomen-irradiated group cannot explain the reduced longevity as measured by median survival, for only 1 rat of the 16 dying during the first 18 months postirradiation developed this lesion (table III). Nephrosclerosis was nearly absent during the 17.5-month period when 50 percent of the upper abdomen-irradiated rats died. Irradiation-induced malfunction of the kidneys, or of some other organ located in the upper abdomen such as the adrenal, may still be specifically related to shortened longevity without there being histologic evidence of this disturbance.

INCIDENCE OF NEOPLASMS

The specific tumors encountered in the various groups of rats are tabulated in table IV. The time distribution of the malignant tumors at death is further indicated in table V where the incidence of malignancy is tabulated according to 6-month survival

periods. In our previous studies the total incidence of malignancy in the irradiated female animals of this Wistar strain did not exceed that observed in the controls when the latter were allowed to live into old age (2). In the smaller number of animals of the present series the high tumor incidence in the controls living over 24 months post-irradiation is again apparent.

TABLE IV

Tissue distribution of benign and malignant tumors following 1,000 r partial-body and total-body irradiation

Location and type of tumor	Extent of shielding				Control
	Head	Upper abdomen	Entire body except upper abdomen	None	
Breast - Adenoma	8	10	6	9	4
Carcinoma		2			
Ovary - Benign	6	2	1	4	1
Malignant					1
Lung - Benign		1	1		
Malignant					1
Lymphoma					1
Disseminated	1	2	2		2
Pituitary		2	2		2
Stomach - Malignant					1
Pancreas - Islet cell			2	1	
Liver - Hemangioma	1	1	2	1	
Kidney - Benign	1	1	2		
Malignant			1		
Heart - Benign	1				
Peritoneum - Malignant		1	1		
Soft tissue sarcoma	1				
Adrenal adenoma	1				
Pudendal gland - Adenoma	1	2			
Carcinoma		1			
Skin of jaw - Carcinoma		1		1	
Uterus - Malignant		1			
Bladder - Cystadenoma		1			
Salivary gland - Adenoma				1	
Number of malignant tumors	2	8	4	1	6
Number of benign tumors	19	20	16	16	7
Number of rats	25	28	32	17	32

Our previous experience with neoplasms in this strain of female Wistar rats indicates that a wide variety of tumors may be expected in old animals. Irradiation in our hands has probably not specifically increased the incidence of any given tumor type with the exception of ovarian tumors (2, 3). The present data are consistent with this generalization.

Choice of areas of the body to be protected from irradiation by lead shielding in these studies was made with the intent of observing primarily the effects of selective partial shielding upon the incidence of nephrosclerosis. Limited information regarding the location of malignant neoplasm with reference to the radiation field can also be obtained. The upper abdomen - irradiated and upper abdomen - shielded groups offer the best opportunity for comparison. When the entire body with the exception of the upper abdomen was irradiated (81.9 percent of total body weight), five malignant tumors were observed to arise within the irradiation field. The other three malignant tumors observed in this group were either widely disseminated with primary site uncertain or were located too close to the margin of the shielding to be placed with certainty either within or outside the radiation field. When only the upper abdomen received irradiation (18.1 percent of body weight), one kidney malignancy was primary within the radiation field, but the location of the other three malignant tumors was indeterminant for the same reasons as given above. In this study no malignant tumor was observed to arise in the irradiated rats from tissues definitely shielded during the irradiation exposure.

DISCUSSION

Longevity, as we observe it in our own species and in the laboratory animal, is influenced by the lethal effects of specific diseases and the consequence of aging. To separate aging from all disease states is a difficult matter. Processes not many years ago considered as inevitable and normal consequences of advanced years such as, for example, arteriosclerosis are now viewed as the result of suboptimal environment or abnormal physiology, or both. In practice when we have eliminated all *known* effects of specific disease, those tissue changes that are left in association with advanced age are referred to as the changes of aging.

In human pathology it is often easy to recognize death as the result of some clearly morbid process. However, in very old individuals of 90 or 100 years, often the absence of marked chronic disease of all organ systems is the conspicuous finding. This relative freedom from severe chronic disease in some

TABLE V

Incidence of malignant tumors at autopsy during various periods of postirradiation survival following 1,000 r hypoxic total-body or partial-body irradiation

Extent of body shielding	Months postirradiation survival								Total	
	7 - 12		13 - 18		19 - 24		25 - 30			
	Tumors	Deaths	Tumors	Deaths	Tumors	Deaths	Tumors	Deaths	Tumors	Deaths
Upper abdomen	1	5	3	12	4	9	–	–	8	26
Head	0	3	1	12	1	7	–	–	2	22
Entire body except upper abdomen	0	6	1	9	3	16	–	–	4	31
None	0	6	0	6	1	5	–	–	1	17
Controls. No irradiation	0	1	0	2	2	12	4	16	6	31

elderly people no doubt in part explains the occasional long survival of such individuals. Deaths under such circumstances are usually caused by bronchopheumonia as a terminal illness. The ability to resist such terminal infections is obviously an important characteristic of the individual with the capacity for long life.

The nonirradiated female Wistar rats, as observed in this laboratory, have had a mean survival of 28 months with many of them living to 36 or 40 months. Even at this advanced age, for the laboratory rat, the peak in the mean weight curve is not yet reached. Most terminal illnesses in these old rats are readily explained by acute inflammations, presumably of infectious origin, involving vital organs such as the lungs, pericardium, or peritoneum. When death occurs, most often by pneumonia, the cardiovascular renal system by microscopic examination appears to have ample reserve. Our rats have been remarkably free of severe generalized so-called "degenerative" changes of the circulatory system that have so complicated the distinction between disease and aging in the human species. We have not observed significant arteriosclerosis of large or middle-sized vessels and we rarely have observed inflammatory vascular disease such as periarteritis or generalized arteriolar disease in the control animals.

In contrast, in older nonirradiated control animals both benign and malignant tumors commonly create conditions not compatible with life. When these tumors are excluded, longevity in our rats appears to be largely a matter of resistance to infection. If one assumes that this resistance to infection is related in some obscure manner to the age of the animal, then our longevity statistics also bear on the process of aging.

The pattern of disease in the postirradiated rat is remarkably similar to that observed in the nonirradiated controls. Inflammatory diseases of the thoracic organs and benign and malignant tumors dominate. In addition, we occasionally have superimposed a severe renal disease involving primarily glomeruli and renal vessels of small caliber which appears to be related in some fashion to irradiation-stimulated hypertension.(5).

Inclusion of the kidneys within the radiation field has so far been necessary in these studies to produce this nephrosclerosis in the irradiated animal. We have not yet, however, produced this lesion in irradiated rats without the concomitant existence of hypertension when adequate prior blood pressure data have been available. Also, the hypertension appears to antedate the development of nephrosclerosis (5). Unfortunately, the blood pressure determinations in the present study were too sporadic to provide additional information on this subject.

Rats of the present study developed nephrosclerosis following irradiation of the upper abdomen alone, but failed to do so when the upper abdomen was protected from irradiation by lead shielding. Organs other than the kidney are involved in these upper-abdomen, radiation-shielding studies. We have, for example, not yet excluded the adrenal as the organ in the upper abdomen responsible for postradiation hypertension. Studies in progress where we have selectively irradiated only the adrenals or kidneys following operative exposure of these organs are not yet complete. Possibly irradiation of the kidneys is necessary to produce the hypertensive state that is a prerequisite for the development of the histologically evident renal disease following radiation at this 1,000 r hypoxic dose level.

The peak of the animal's capacity to increase in size is also reached in these postirradiated rats in contrast to the control group whose mean body weight increases throughout the life span. In the postirradiated female Wistar rats of this report, the critical characteristic of shortened longevity, which is related to a decreased resistance to infection, appears also to be closely associated with a decline in net capacity for accumulation of new tissue. Studies of growth based on skeletal structure have not yet been attempted.

Existing data on the late effects of radiation of less than the total body are particularly meager. Kaplan's (6) study of the effect of partial-body irradiation in mice was directed toward the incidence of lymphomas rather than the general problem of late effects of radiation exposure. The recent study of Maisin et al. (4) provides the bulk of the published data on the

rat. Kallman and Kohn (7) have also demonstrated a life-shortening effect of partial-body irradiation in the mouse.

Following 600 r total-body radiation ($LD_{50/30}$) Maisin et al. (4) observed a post-30-day 50 percent survival of 10.8 months in contrast to the 18 months of the controls. In their hands shielding an 8.0 cm.^{2} region of the chest ($LD_{2.8/30}$) or mid-abdomen ($LD_{12.8/30}$) failed to appreciably lengthen the life span of the post-30-day survivors, although admittedly the proportions of the body shielded are small.

Similar partial shielding studies following 850 r in Maisin's report (4) cannot be compared to total-body irradiation because of absence of long-term survivors of the 850 r total-body exposure. Nevertheless, in experiments where the total body, except for the abdomen, has been shielded from the 850 r dose, longevity has been reduced substantially from that observed in the nonirradiated controls. Our data, although not statistically significant, then support the findings of Maisin indicating that irradiation to the abdomen alone is followed by reduction of life span in the post-30-day survivors. Maisin suggests that this shortened longevity is related to diseases of the abdominal organs, but autopsy details are lacking.

When the total body is irradiated, if the injurious effects are in part nonremedial, it would be logical to assume that each of the individual tissues would be the seat of damage produced by residual ionization. The sums of these damages in all tissues could be injurious to the total organism by impairment of the individual specific functions unique to the vital organ concerned. It is also conceivable, since there are no autonomous organs in the body, that ionization tissue damage also has a less specific aspect relating rather more to some common denominator that is present in all tissues, yet essential and available to the entire integrated animal body. In the latter case the summation effects of total-body irradiation damage would be less organ dependent and more likely related to total weight of all tissues included within the radiation field.

If regions of the body containing vital organs such as the brain, heart, or liver were exposed to radiation doses sufficiently large to cause tissue damage as the result of delayed vascular injury, the influence of local irradiation upon longevity might be a combination of both organ specific and nonspecific mechanisms. In its effects on longevity, the 1,000 r hypoxic radiation used in these studies is equivalent to approximately 425 to 500 r delivered in normal oxygen tension (2). Doses of this relatively small size have not caused a generalized severe sclerosis of vessels although the renal lesion observed in these studies in association with hypertension (5) is possibly related to

TABLE VI

Incidence of nephrosclerosis and postirradiation survival after 1,000 r hypoxic total-body or partial-body irradiated

Percent of body irradiated	Portion shielded	Incidence of nephrosclerosis	Median survival in months	Mean survival in months
100	None	6/17	12.0	12.0
87	Head	14/25	13.5	13.0
77	Upper abdomen	0/28	14.5	12.5
23	Entire body except upper abdomen	7/32	17.5	17.0
0	None - nonirradiated controls	1/31	22.0	20.5

clandestine vascular injury. The unilateral renal damage in rats, reported by Maisin (4), following a dose of 850 r in air suggests that the hypoxic 1,000 r (used in our study) may be only slightly below the threshold for histologically demonstrable direct renal radiation injury.

Nevertheless, when only a portion of the body is irradiated with 1,000 hypoxic r we also observe reduced longevity, although of lesser degree than that following total-body irradiation. This, in part, may possibly be explained by the accelerated appearance of malignant tumors within the irradiated area. In the case of upper abdominal irradiation it may be explained in some cases by nephrosclerosis, although in this study the nephrosclerosis observed did not appear sufficiently soon to affect appreciably the median survival figure. But the life span of rats that have received partial-body irradiation and are free of both tumors and nephrosclerosis is also shortened. Their terminal illnesses are similar to those of the totally irradiated rats and the controls. They largely die of pneumonia. Possibly we are concerned here with a submicroscopic injury to some organ such as the adrenal or a nonspecialized type of universal tissue damage of the type mentioned earlier.

Consequently, we have searched for a possible relationship between the reduction in life span in our partially shielded experiments and the proportion by weight of the total body receiving the ionization challenge. It may be fortuitous that shielding the head, or the upper abdomen, or 81.9 percent of the total body increases longevity by degrees roughly proportional to the weights of these regions. The increased longevity may be related only to more normal specialized function of these regions, all of which contain organs vital to survival. It is also possible that the sum total of all ion pairs formed by radiation absorption in all parts of the body regardless of locus is a critical factor bearing on aging.

We do know that animals irradiated in the upper abdomen only do not all die of demonstrable upper abdominal disease as determined by standard autopsy technics. The proof of the existence of a form of late radiation damage capable of influencing longevity but not related to known functions of specific organs obviously will depend upon more data. Longevity following the selective irradiation of portions of the body clearly containing no organs known to be vital to survival will be of interest. Such studies are in progress.

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